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23 July 1998

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Dr. Room 1-23
Rockville, Maryland 20857

4382 '98 JUL 28 A9:49

Re: Proposed rule: "Dissemination of Information on Unapproved/New Uses for Marketed Drugs, Biologics, and Devices";
Food and Drug Administration
21 CFR Parts 16 and 99
Docket No. 98N-0222

This letter represents the response of the Ohio Regulatory Forum to FDA's request in the 8 June 1998 Federal Register for comments regarding the proposed rule referenced above.

The Ohio Regulatory Forum (ORF) is a statewide coalition of medical device, pharmaceutical and biotechnology companies. The Forum serves to educate and inform its constituents and provides a medium for the review of, and comment on, regulatory issues and proposals put forth by the Food and Drug Administration, and other regulatory agencies as appropriate.

In general, it is the opinion of ORF that the proposed rule is reasonably well conceived and is consistent with Section 401 of the FDA Modernization Act of 1997 and the general purpose of the Federal Food, Drug, and Cosmetic Act. While there are no significant issues being addressed by the ORF at this time, we are providing comments on some aspects of the proposed rule as follows:

COMMENT 1 - § 99.101(a)

The proposed rule currently states the following: "[a] manufacturer may disseminate written information concerning the safety, effectiveness, or benefit of a use not described in the approved labeling for an approved drug or device or in the statement of intended use for a cleared device..."

This statement may imply that information may be disseminated only in printed, hard copy form. The dissemination of information electronically is a very practical matter, but one which does not appear to be addressed directly in the proposed rule. With the advent of electronic journals and portable document format files, it is also possible to disseminate such information electronically. FDA both accepts electronic premarket submissions from industry and transmits its own important information (e.g., proposed rules, guidance documents, etc.) electronically utilizing its site on the World Wide Web, and realizes significant gains in efficiency in both applications. The advertising and labeling requirements that apply to written materials regarding FDA-regulated products apply equally to the same materials in electronic form. There are also means for manufacturers to control and document who receives information electronically, e.g.,

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via restricted access to web pages. The proposed rule should facilitate the dissemination of information, whether electronically or in the printed form.

Please clarify whether the use of the term "written" is intended to preclude the use of any other form of information dissemination, including electronic dissemination.

COMMENT 2 - §§ 99.201(a)(4)(ii)(A) and 99.301(b)(1)

The proposed rule currently states the following: "[t]he protocols shall comply with all applicable requirements in parts 312 of this chapter (investigational new drug applications) and 812 of this chapter (investigational device exemptions)." Also, section II.C. of the Description of the Proposed Rule states the following: "[t]his means that the protocols must be sent to the appropriate review divisions within [CDER], [CBER], or [CDRH]. The protocols will be reviewed as an original IND or IDE or an amendment to an existing IND or IDE."

The above language is unclear regarding what information must actually be submitted to FDA, and the rule's use of the term "protocol" contributes to this lack of clarity. In accordance with 21 CFR § 812.25(b), a "protocol" is the written document that describes the methodology to be used in a medical device clinical study. Under the IDE regulation, a protocol is only one of the components of an investigational plan, and thus is only one of the required documents submitted as part of an IDE application in accordance with § 812.20(b).

Please clarify whether § 99.201(a)(4)(ii)(A) actually means that the manufacturer who has only planned studies and wishes to disseminate information under this rule must submit a complete IND or IDE application (for a significant risk device) in accordance with parts 312 or 812, respectively, in addition to the information required as part of a submission under this rule. If this is the case:

1) Please further clarify the procedures manufacturers are to follow when making a submission under § 99.201(a)(4)(ii)(A), including the required physical organization of the document(s) and whether the IND or IDE is to be sent by the manufacturer to the designated FDA office as specified under § 99.201(c) or to the "appropriate review division."

2) Please clarify § 99.301(b)(1) likewise to indicate that FDA will review the IND or IDE application (for a significant risk device) and will notify the manufacturer of the IND or IDE approval, and that, until such notification, the manufacturer must not disseminate the information.

3) Please clarify the submission requirements under § 99.201(a)(4)(ii)(A) and the FDA action requirements under § 99.301(b)(1) with respect to nonsignificant risk devices.

COMMENT 3 - § 99.401(c)(1)

Clarification is requested regarding the point within the supplemental application review process at which FDA may determine that the supplemental application does not contain adequate information for approval of the new use. As it is currently written, the proposed rule implies that

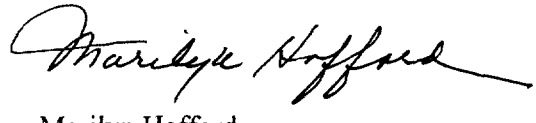
information or clarification regarding initial premarket submissions are commonplace and are usually satisfied by sponsors' amendments to the initial submissions. Clearly, the dissemination of information should cease only upon FDA's determination that a submission is not approvable.

COMMENT 4 - § 99.501(c)

Clarification is requested regarding FDA's definition of "cessation of dissemination" as it may relate to the approval of a supplemental application. Information disseminated under this rule, prior to approval of the supplemental application, may continue to be distributed by the sponsor following approval of the supplemental application. However, such distribution would not constitute "dissemination" under this part, but would be allowed under the approved supplemental application. As such, the requirements for recordkeeping and reports under this part would not apply for the information as distributed under the approved supplemental application.

If you have any questions or require clarification regarding any information provided in this letter, you may contact me directly at 216-229-0400, ext. 114.

Sincerely,



Marilyn Hofford
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